Modulation of dopamine D$_{2L}$ and D$_3$ signalling and trafficking and cytosolic cell surface trafficking by dysbindin

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Abstract: Schizophrenia is a severe neuropsychiatric disorder with many risk factors, both environmental and genetic. In regards to genetic factors, dystrobrevin binding protein 1 (dysbindin) is a susceptibility gene and its levels are reduced in schizophrenia [1]. Further, genetically reducing dysbindin expression enhanced cell surface expression of D$_2$ receptors in frontal cortex [2]. These observations suggest altered control of dopaminergic transmission in schizophrenia by dysbindin. In view of this we investigated the influence of dysbindin overexpression on signalling and cell surface localisation of human (h) dopamine D$_2L$ versus D$_3$ receptors stably expressed in CHO cells.

I. Dysbindin decreases cell surface expression of Dopamine D$_2L$ and D$_3$ receptors in CHO cells

II. Dysbindin decreases inhibitory effect of dopamine stimulation on forskolin-activated adenyl cyclase

III. Dysbindin decreases efficacy of Akt and GSK-3B phosphorylation upon dopamine stimulation

IV. Efficacy of Erk1/2 phosphorylation is decreased by dysbindin overexpression

V. Inhibition of clathrin/caveolar- mediated receptor internalisation attenuates the decreasing effect of dysbindin on D$_2L$ and D$_3$ signalling

VI. Conclusions

VII. References

Figure 6

The schizophrenic. Adapted from www.psych.ox.ac.uk